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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/060,697	01/30/2002	Donald W. Petersen	06317-038003	8553

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EXAMINER	
WITZ, JEAN C	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 11/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	10/060,697	PETERSEN, DONALD W.	
	Examiner	Art Unit	
	Jean C. Witz	1651	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 September 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *15 September 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attached document*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: _____.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Jean C. Witz
Primary Examiner
Art Unit: 1651

Response to Arguments

1. Applicant's arguments filed September 15, 2004 have been fully considered but they are not persuasive for the reasons set forth below.

Applicants again assert that the teaching of the Yim reference must be limited to a suggestion to combine a calcium sulfate hemihydrate-containing substance (CSHS) with the formulation of U.S. Patent 5,171,579 which is a formulation of osteogenic proteins, a blood clot and a porous particulate polymer matrix. This is merely one embodiment of the disclosure of Yim and Applicants' assertion fails to address, for example, the statement found at col. 2, lines 27-31, found in the Summary of the Invention section, which identifies another embodiment of the invention of Yim, specifically "[y]et another embodiment of the present invention comprises formulation of osteogenic protein and a suitable quantity of a CSHS. The formulation may optionally include other protein sequestering agents, particularly cellulosic materials." The formulation referred to by Applicants is merely one embodiment of several disclosed by the Yim patent and the teachings of a U.S. patent are not limited solely to a single or even the preferred embodiment. Therefore, it is clear that Yim does suggest the combination of osteogenic proteins, CSHS and a cellulosic material (as defined at col. 7 and within the scope of the claimed "plasticizing substance") for repair of bone. One of ordinary skill in the art is well aware that compositions that contain osteogenic proteins include demineralized bone matrix (DBM) and that demineralized bone matrix is a common source of these proteins; in fact, this is one of the reasons why O'Leary uses DBM in his formulation, i.e. as a source of these proteins. See O'Leary at col. 1, lines

15-21. It is not seen how the disclosed benefits of inclusion of CSHS to the embodiment discussed by Applicants would not also be expected to be imparted to all of the embodiments discussed by Applicants in the Summary of the Invention, including the embodiment discussed above. Further, given that Yim's teachings suggest a composition comprising osteogenic proteins, CSHS, a cellulosic material and a mixing solution to activate the CSHS, and given that broadest reasonable interpretation of a composition that comprises osteogenic proteins includes within its scope demineralized bone matrix, the disclosure of Yim actually suggests a composition that contains four of the five components claimed by Applicants. Finally, it is noted that Applicants' claims recited "open" claim language, allowing for the inclusion of other components. Therefore, Applicants' assertions regarding the Yim reference have not been found to be persuasive.

Regarding the O'Leary patent, Applicants assert that "there is nothing in the O'Leary reference to suggest a problem with moldability, consistency, etc. of the formulation described therein that might lead one of ordinary skill in the art to seek an additive to address such a problem. Yim suggests that addition of CSHS improves moldability and consistency bone repair formulations, including those that already contain protein sequestering agents which are the same as the "plasticizing substance" of the instant claims. Applicants focus on the "flowability" already present in the O'Leary reference and suggest that "one of ordinary skill in the art would not view an additional ingredient as necessary to improve moldability, consistency, etc. of the O'Leary formulation." It is respectfully submitted that the quality of flowability is not identical to

the quality of moldability. It is clear from the teaching of Yim that the activation of the CSHS results in a change of state upon the hydration of the calcium sulfate such that the hydrated calcium sulfate hardens over time and during this period, the moldability of the composition improves. The formulation of O'Leary, once formulated in the desired state of "flowability", does not similarly change its state and its moldability is static and does not improve. Therefore, a flowable composition may have its moldability improved by the addition of the CSHS.

Applicants also appear to be suggesting that O'Leary must identify the problem in order to provide the motivation to solve it; however, there is no requirement in the patent law as to which specific piece of prior art provides the motivation to combine the references. "There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art." In re Rouffet, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). So long as at least one of the prior art references provides the motivation, the requirements of the statute are met.

Further, Applicants also err in requiring that any prior art document must explicitly identify a problem to be solved in another specific formulation in order to provide motivation. Yim shows that bone repair compositions that do not contain CSHS will have improved moldability upon the inclusion of the CSHS and provides a reasonable expectation of success based upon the known properties of CSHS. This teaching is not negated simply because Yim does not identify all specific extant bone repair

formulations that do not contain CSHS. Again, such a requirement is not consistent with existing patent law and would, in fact, be onerous.

Further, the motivation to improve a result with a superior formulation does not require a recognized defect or problem; there is no need for the formulation of O'Leary be inoperable or unuseful to be improved upon but instead there is a need for a disclosure that would suggest to one of ordinary skill in the art that the formulation of O'Leary would be improved if CSHS were added, which is done by the disclosure of Yim. The level and degree of efficacy of the O'Leary formulation and the level and degree of improvement expected by the claimed (and suggested) invention is not mandated by the claims.

Finally, Applicants assert that "there is not motivation to combine the teachings of the Wironen reference with the teachings of either O'Leary or Yim." Applicants assert that the composition of Wironen is "so fundamentally distinct from the composition described in the Yim and O'Leary references that one of ordinary skill in the art would clearly view such differences as weighing against the combination suggested by the Examiner." It remains unclear as to the basis of this conclusion in view of the disclosure of Wironen. The formulation of Wironen, at its broadest, is a composition of gelatin and demineralized bone matrix. O'Leary, drawn to a flowable composition comprising a demineralized bone powder, explicitly states that a thickener is included and gelatin is expressly recited as one such thickener. See col. 4, line 2. Therefore, it is not seen how Wironen discloses such a "fundamentally distinct" composition especially in view of

the fact that the compositions both O'Leary and Wironen may contain the same ingredients and are used for the same purpose.

Applicants again assert that Wironen may not be combined with O'Leary because Wironen actually refers to O'Leary at page 3; Applicants suggest that this is a teaching away from the formulation of O'Leary. However, the reference of Wironen to the formulation of O'Leary appears merely speculative, i.e. "[I]t is considered likely that this material is rapidly washed away from the implant location . . ." and the rejection of record is not limited solely to the combination of Wironen and O'Leary. As already discussed above, the contribution of Yim is specifically devoted to this issue and as such, one of ordinary skill in the art would not consider the discussion of the O'Learly formulation in the Wironen reference alone, in a vacuum, but instead would take it in view of the disclosures of all three references. In that vein, the interpretation of the Wironen reference that "would only suggest to one of ordinary skill in the art that cancellous bone chips could be useful as an additive in a gelatin-based composition that exhibits thermoreversible gelation properties" is improper for the reasons set forth above and further because Wironen specifically provides the function of the cancellous bone chips (i.e. filling larger bone voids and when not demineralized, provide an added spectrum of biological properties not exhibited by the other ingredients). One of ordinary skill in the art would not assume that these functions would only be imparted to the specific formulation of Wironen but instead would have a reasonable expectation of imparting other bone repair formulations with these functions by including cancellous

bone. This expectation is explicit because the reference statess that the addition of these ingredients imparts an improved quality to the disclosed formulation of Wironen.

Finally, Applicants again argue that there are no express teachings for the specific formulations set forth in the claims nor are there any teachings regarding the amounts of cancellous bone to be included. However, Applicants do not address the statements made by the Examiner in the previous office actions. As stated previously, the general amounts of both the demineralized bone matrix and the cellulose material are taught by the references. The optimization of the amount of calcium sulfate and mixing solution to be further included is deemed well within the skill of the practitioner at the time the invention was made as it is clear that the amount of calcium sulfate is directly related to desired rate of set up of the composition, i.e. the more calcium sulfate used, the faster the composition will set up and harden. Further, it is clear that the amount of mixing solution is inversely related to the desired set up time and directly proportional to the ultimate consistency of the composition, i.e. the more mixing solution used, the more dilute the calcium sulfate and the slower the set up time but the more liquid the composition will become. Therefore, the Examiner has provided the evidence that optimization is well within the skill of the practitioner. With regard to the cancellous bone, the optimization of amounts is equally within the skill of the practitioner. Wironen discloses the purposes for the inclusion of the cancellous bone in bone implant compositions – to fill larger bone voids; therefore, optimization of amounts of cancellous bone to achieve these purposes are deemed also well within the skill of the practitioner. It remains unclear as to how the practitioner would not be able to determine the size of

the void to be filled and add as much cancellous bone as deemed necessary to fill the void. Finally, Applicants have provided no evidence of unexpected or surprising results in the use of any given formulation.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jean C. Witz whose telephone number is (571) 272-0927. The examiner can normally be reached on 6:30 a.m. to 4:00 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jean C. Witz
Primary Examiner
Art Unit 1651